A Dissertation on

A STUDY ON CLINICAL SPECTRUM, BIOCHEMICAL AND HEMATOLOGICAL PROFILE OF ACUTE FALCIPARUM MALARIA

Submitted to

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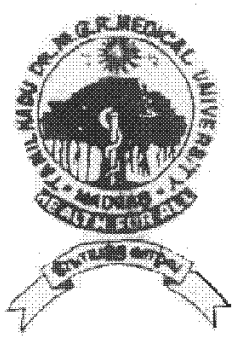
BRANCH - I



KILPAUK MEDICAL COLLEGE,
CHENNAI

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CERTIFICATE

This is to certify that "**A STUDY ON CLINICAL SPECTRUM, BIOCHEMICAL AND HEMATOLOGICAL PROFILE OF ACUTE FALCIPARUM MALARIA"** is bonafide work done by **Dr.S.RAJESH KUMAR** Post Graduate Student Department of General Medicine Kilpauk Medical College, Chennai-10 under my guidance and supervision under my guidance and supervision in fulfillment of the regulation of the Tamilnadu **DR.M.G.R. MEDICAL UNIVERSITY** for the award of MD Degree Branch – I (General Medicine) during the academic period from 2004 to 2007.

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DECLARATION

I, **Dr.S.RAJESH KUMAR**, solemnly declare that the dissertation titled ""**A STUDY ON CLINICAL SPECTRUM, BIOCHEMICAL AND HEMATOLOGICAL PROFILE OF ACUTE FALCIPARUM MALARIA"** was done by me at Government Kilpauk Medical College and Hospital during 2004-2005 under the guidance and supervision of my unit **Prof.S.R.SAKUNTHALA M.D.,**

The dissertation is submitted to **The Tamil Nadu Dr.M.G.R. Medical University** towards the partial fulfillment of requirement for the award of M.D. Degree (Branch – I) in General Medicine

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CONTENTS

INTRODUCTION

Malaria is a major international public health problem. Malaria is seen in all the continents to a certain extent. At present it is endemic between the Tropics of Cancer and Capricorn. Malaria affects more than 500 million people and cause 2-3 million deaths each year. Despite its already enormous toll of suffering, deaths due to malaria are increasing as a consequence of drug resistance.[1]

The global resurgence of malaria can be attributed to a variety of factors – insecticide resistance in the Anopheles mosquito, resistance of plasmodium falciparum to affordable first line antimalarials, deterioration of national control programs and increased movement of populations secondary to increase in international travel and tourism.

Plasmodium falciparum is the most common cause of severe and life threatening malaria. It affects all age groups although the reported mortality varies considerably depending upon the age, immunity, clinical complications and access to appropriate treatment.[2]

The mortality is higher in adults with severe falciparum malaria than in children with similar disease[3] as evidenced by the fact that mortality amongst South East Asian adults with renal failure due to severe malaria is 45% while the mortality amongst Kenyan children with severe anemia is only 1%.[4] Intensive care with facilities for ventilation and haemodialysis appears to reduce the mortality.[5]

The remedies to reverse the present situation are

1) Better sanitation, engineering solutions to mosquito breeding

2) Proper town and house planning

3) Drug research along with the development of newer insecticides.

4) Vaccine.

The first two options are highly capital intensive and it is unlikely that the states endemic for malaria would be in a position to afford them. It is nearly a decade since any new antimalarial drug was developed. The low paying capacity of malaria victims makes drug development unattractive for pharmaceutical firms. Efforts are being made to remedy the situation by setting up organizations like the Medicines for Malaria Venture, Roll Back Malaria consortium.

Among the South East Asian countries, India alone contributes more than 80% cases of malaria and plasmodium falciparum accounts for 35 – 40 % of cases.[6] In an endemic area, apart from classical presentations of fever with chills and rigor of short duration, not uncommonly a completely different presentation may be encountered because of multisystem involvement in the disease process.

Therefore the study was carried out in acute falciparum malaria with objective of noting common presentations, atypical presentations if any, complications, hematological and biochemical abnormalities and their correlation with clinical severity and prognosis.

AIMS OF THE STUDY

1) To find out common clinical presentations and also atypical presentation if any of acute plasmodium falciparum malaria.

2) To assess life threatening complications of severe malaria.

3) To collect a detailed hematological and biochemical profile in acute falciparum malaria with objective of noting its abnormalities and correlation if any with clinical severity and prognosis.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND

Malaria is probably one of the oldest diseases known to mankind. Man and malaria seem to have evolved together and it has been known to mankind for millennia. It was always part of ups and downs of nations, of wars and of upheavals. Mentions of this disease can be found in the ancient Chinese, Indian and Egyptian manuscripts. The disease supposedly had its origins in the jungles of Africa, where it is still very much rampant.

In 1696, Morton presented the first detailed description of the clinical picture of malaria and its treatment with cinchona. In 1880, Laveran, a French physician first identified the causative agent for human malaria. In 1885, Golgi identified P.vivax and P.malariae. In 1889, Sakharov and in 1890, Marchiafava and Celli identified P.falciparum. In 1894, Manson hypothesized that mosquitoes transmit malaria.

In 1897, Sir Ronald Ross demonstrated the malarial oocysts in the gut tissue of female Anopheles mosquitoes proving the fact that Anopheles mosquito were the vectors for malaria.

Chloroquine was synthesized and studied under the name of Resochin by the Germans as early as 1934. From them onwards lot of research into malarial parasite, host interactions, newer drugs and vaccine developments have come into effect.

GLOBAL TRENDS IN MALARIA

- Malaria presents a public health paradox. Malaria prevails in Africa, South Asia and the Amazon and continually threatens the developed world. It thrives on poverty, population movement, and environmental disruption, all of which are in abundant supply in its current tropical homelands. Malaria is endemic in 91 countries with about 40 % of world's population at risk of acquiring the infection. Every year 300 million to 500 million people suffer from this disease[1] (90% of them in sub-Saharan, Africa, two – thirds of remaining cases occur in six countries – India, Brazil, Sri Lanka, Vietnam, Colombia, and Solomon Islands.)

- WHO forecasts a 16% growth in malaria cases annually

- Malaria kills in 1 year what AIDS, killed in 15 years. If 5 million have died of AIDS in 15 years, 50 million have died of malaria.

- Malaria ranks third among the major infectious diseases in causing deaths – after pneumococcal acute respiratory infections and tuberculosis.

- It accounts for 2.6% of the total disease burden of the world. It is responsible for the loss of more than 35 million disability – adjusted life years in the world.

- Estimated global annual cost (in 1995) for malaria: US$ 2 billion (direct and indirect costs, including loss of labor).

- Estimated world wide expenditure on malaria research: US$ 58 million, one thousandth of the US$ 56 billion spent globally on health research annually.

STATUS OF MALARIA IN INDIA

In India, with the implementation of Modified Plan of Operation in 1977, the upsurge of malaria cases dropped down from 6.74 million cases in 1976 to 2.1 million cases in 1984. Since then the epidemiological situation did not show any great improvement which seemed to have reached a plateau causing concern[7.]

Since 1997, there is a declining trend in annual malaria incidence in the country. During the year 2003 about 1.65 million cases reported with 943 deaths. There were 0.7 million cases of P. falciparum malaria[7]. The disease is grossly under – reported.

Malaria has been a serious problem in North – eastern states contributing 8.5 to 11 per cent of total malarial cases and 13 to 15 percent of total malarial mortality in the country[7]

MALARIAL SITUATION IN INDIA[7]

Year	Cases in million		Deaths	API
	Total cases	P.falciparum		
1996	3.04	1.18	1010	3.48
1997	2.66	1.04	879	2.86
1998	2.22	1.03	664	2.44
1999	2.28	1.14	1048	2.41
2000	2.03	1.05	932	2.09
2001	2.09	1.01	1005	2.06
2002	1.84	0.89	973	1.80
2003	1.64	0.70	943	1.62

API-- Annual Parasitic Index

STATEWISE MALARIA SITUATION IN INDIA 2002 AND 2003[7]

STATE	2002		2003	
	POSITIVE CASES	DEATHS	POSITIVE CASES	DEATHS
Andhra Pradesh	38053	0	35090	3
Arunachal Pradesh	46431	0	33366	0
Assam	89601	72	55375	38
Bihar	3683	2	2550	1
Chhattisgarh	235434	3	53093	0
Goa	16818	15	11370	1
Gujarat	82966	17	113372	34
Haryana	936	0	4336	0
Jharkhand	126589	31	112740	13
Karnataka	132584	33	99889	22
Kerala	3360	8	2380	4
Madhya Pradesh	108818	30	93780	22

STATE	2002		2003	
	POSITIVE CASES	DEATHS	POSITIVE CASES	DEATHS
Maharashtra	45568	43	62969	85
Manipur	1268	9	2589	17
Meghalaya	17918	41	16503	38
Mizoram	7859	35	7293	49
Nagaland	3945	0	3370	0
Orissa	473223	465	417276	333
Punjab	250	0	377	1
Rajasthan	68627	11	142738	66
Tamil Nadu	34523	0	43382	0
Tripura	13319	5	13577	9
Uttar Pradesh	90199	0	81853	0
West Bengal	194421	152	232846	207
Total	1842019	973	1647378	943

EPIDEMIOLOGY

Like any other disease, natural transmission of malaria depends on the presence of and relationship between the three basic epidemiologic factors: the agent the host and the environment. While the malarial parasite is the agent of infection, the female anopheles mosquito is the agent of transmission.

There are about 400 species of anopheline mosquitoes throughout the world, approximately 80 can transmit malaria, 66 are considered natural vectors, and about 45 are important vectors.[8] In India 9 species out of 45 anopheline species have been incriminated as malaria vectors[7].

The principal determinants of epidemiology of malaria are the number (density), the human – biting habits, and the longevity of the anopheles mosquito vectors. More specifically, the transmission of malaria is directly proportional to the density of the vector, the square of the number of human bites per day per mosquito, and tenth power of the probability of the mosquito's surviving for 1 day. Mosquito longevity is particularly important; it must survive for > 7 days.[9]

MALARIAL TRANSMISSION CYCLE FROM MOSQUITO TO HUMAN

The life cycle of the malarial parasite comprises of an endogenous asexual phase (schizogony) with multiplication in the human host and an exogenous sexual phase (sporogony) with multiplication in anopheles mosquitoes.

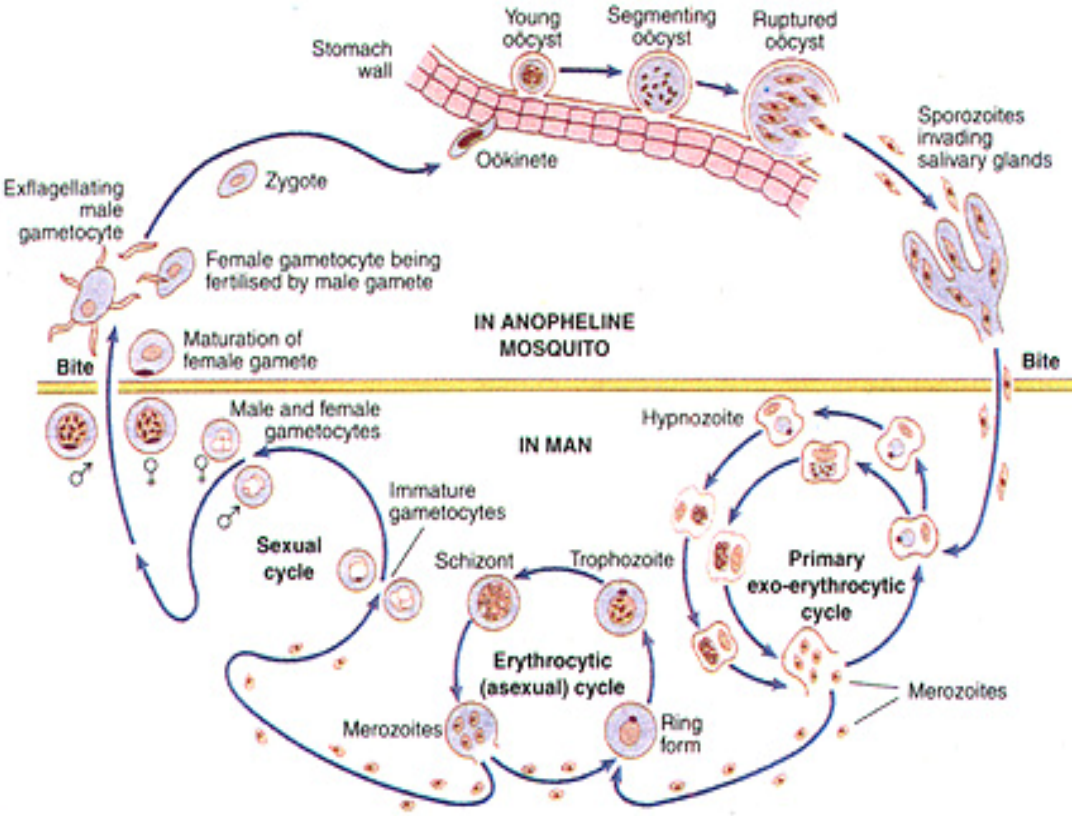
Young oöcyst
Segmenting oöcyst
Ruptured oöcyst
Stomach wall
Oökinete
Sporozoites invading salivary glands
Exflagellating male gametocyte
Zygote
Female gametocyte being fertilised by male gamete
IN ANOPHELINE MOSQUITO
Bite
Maturation of female gamete
Bite
Male and female gametocytes
IN MAN
Hypnozoite
Immature gametocytes
Sexual cycle
Schizont
Trophozoite
Primary exo-erythrocytic cycle
Erythrocytic (asexual) cycle
Merozoites
Merozoites
Ring form

FIG.1

ASEXUAL PHASE IN THE HUMAN HOST

TISSUE SCHIZOGONY (PRE - ERYTHROCYTIC STAGE)

This phase starts with the inoculation of the parasite into the human blood by bite of the female anopheles mosquito. Within half an hour the sporozoites reach the liver and invade the liver cells. The mechanism of targeting and invading the hepatocytes wih such rapidity is not yet clear. Within the liver cells, the sporozoite starts their intracellular asexual division. A single sporozoite eventually may produce 10,000 to 30,000 daughter merozoites.[9] The swollen liver cell bursts, discharging motile merozoites into the blood stream. These then invade the RBCs and multiply 6 – 20 fold every 48 to 72 h[9]. After entry into the blood stream merozoites rapidly invade erythrocytes and become trophozoites.

ERYTHROCYTE SCHIZOGONY

Within the red cell, the parasite develops through the stages of rings, trophozoites, early schizonts, each mature schizont consisting of thousands of erythrocytic merozoites. These merozoites are released by the lysis of the red blood cells and they immediately invade uninfected cells. The intra erythrocytic cycle takes about 48 hours for P. falciparum[9]. A small proportion of the merozoites in the red blood cells undergo transformation into gametocytes – male and female. Mature gametocytes appear in the peripheral blood after 8 - 11 days of the primary attack in P. falciparum.

SEXUAL PHASE IN THE MOSQUITO

SPOROGONY

The gametocytes continue their development in the mosquito. The male and female gametes fuse and form into a zygote. This transforms into an ookinte[9], penetrates the gut wall and becomes an oocyst. The oocyst divides asexually into numerous sporozoites which reach salivary gland.

ERYTHROCYTE CHANGES IN MALARIA

After invading an erythrocyte, the growing malarial parasite progressively consumes and degrades intracellular proteins, principally hemoglobin. Toxic heme is polymerized to biologically inert hemozoin or malarial pigment. It alters the RBC membrane and makes RBC more irregular in shape, more antigenic and less deformable[9]. In P. falciparum infections, membrane protuberances appear on the erythrocyte surface toward the end of the first 24 h of the asexual cycle. These knobs extrude adhesive protein (pfEMP1)[9] that mediates attachment to receptors on venular and capillary endothelium – an event termed cytoadherence. ICAM-1 is probably the most important vascular receptor in the brain, chondroitin sulfate B in placenta, and CD 36 in most other organs.

At the same stage these infected RBCs may also adhere to uninfected RBCs to for rosettes and to other parasitized erythrocytes – agglutination[8]. The process of cytoadherence, rosetteing and

agglutination are central to pathogenesis of falciparum malaria. They result in sequestration of RBCs in vital organs where they interfere with microcirculatory flow and metabolism.[10,11]

CLINCAL FEATURES

The first symptoms of malaria are nonspecific: the lack of a sense of well – being, headache, fatigue, abdominal discomfort, and muscle aches followed by fever. The classical malarial paroxysms, in which fever spikes, chills, and rigor occur at regular intervals are relatively unusual in falciparum and suggest infection with P.vivax.[9] The fever of falciparum malaria is irregular at first and the temperature often rises above 40^0 c in conjunction with tachycardia and sometimes delirium.

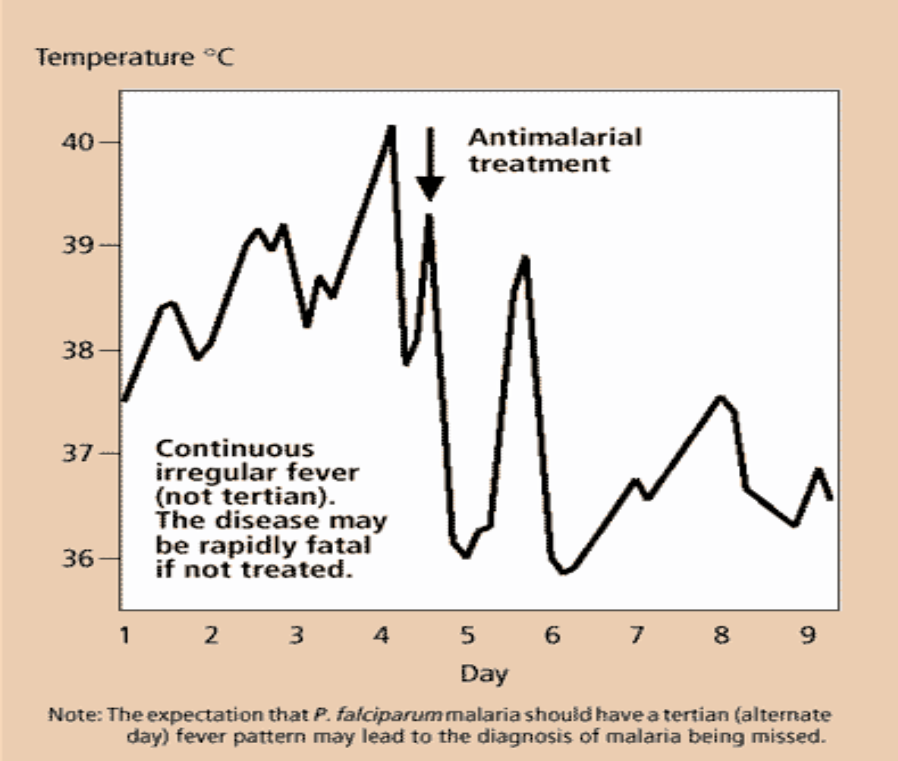

FIG.2

Falciparum malaria presents with protean manifestations and is associated with a variety of complications and has a high mortality. Plasmodium falciparum in contrast to the benign malarias, may progress to a life threatening multisystem disease. Importantly the affection of renal, haematological, central nervous system adds to the mortality. Pernicious syndrome consisting of anemia, hypotension, haematological parameters and cerebral involvement is seen most commonly in plasmodium falciparum infection.

Sometimes falciparum malaria presents with atypical presentations as evidenced by some of the studies.

Falciparum malaria presenting as a leukaemoid reaction.[12]

In falciparum malaria clinical presentations were dominated by features other fever or the history of fever was totally absent. Some of the presentations were Acute abdomen, urticaria, and unexplained shock. [13]

According to WHO the term severe malaria is defined as the presence of one or more complication in a patient having asexual parasitemia in the peripheral blood smear.[2]

COMPLICATIONS OF FALCIPARUM MALARIA

MALARIAL HEMATOPATHY

Malarial Hematopathy attempts to describe the involvement of one or more hematopoietic cell lines and includes the endothelial

dysfunction that can give rise to a thrombotic microangiopathy that may evolve into a consumptive coagulopathy.

ANEMIA

The pathogenesis of anemia in malaria is multifactorial. Anemia results from accelerated RBC destruction and removal by the spleen in conjunction with ineffective erythropoiesis. In severe malaria, both infected and uninfected RBCs show reduced deformability, which correlates with prognosis and development of anemia[9]. Splenic clearance of RBCs is increased.The cause of dyserythropoiesis is believed to be related to intramedullary cytokine production[8]. Anemia is a common consequence of antimalarial drug resistance, which results in repeated or continued infection[9,14.]

THROMBOCYTOPENIA

Thrombocytopenia is a common occurrence in acute malaria. It has been identified as a key indicator for malaria in patients with acute febrile illnesses. Thrombocytopenia is rarely accompanied by clinical bleeding or biochemical evidence of DIC. Platelet counts rapidly rise with recovery.

The mechanism of thrombocytopenia in malaria is uncertain. Immune – mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelet structure and function have been

described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves.

Thrombopoietin (TPO) is the key growth factor for platelet production and is elevated in states of platelet depletion. TPO serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14 – 21 days of therapy.[15]

Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyperactivity; this is followed by platelet hypoactivity. Platelet hyperactivity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells. The injured platelets undergo lysis intravascularly. The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypoactivity is seen following this phase and returns to normal in 1 to 2 weeks.[15.]

LEUCOCYTE COUNT

Total leukocyte count is usually normal however leukocytosis can occur especially when associated with pernicious malaria and superadded bacterial infections. Leucopenia has also been observed.[16] Increase in the number of atypical lymphocytes has been reported in acute falciparum infection at times leading to false positive serological tests like the widal titres.[17].

LIVER DYSFUNCTION

Mild hemolytic jaundice is common in malaria. Severe jaundice is associated P.falciparum infections, is more common among adults than among children, and results from hemolysis, hepatocyte injury, and cholestasis. When accompanied by other vital organ dysfunction (often renal impairment), liver dysfunction carries a poor prognosis.[9]

Hepatic dysfunction contributes to hypoglycemia, lactic acidosis, and impaired drug metabolism.

The cause of jaundice in a patient of plasmodium falciparum malaria is multifactorial and includes

- Intravascular hemolysis due to destruction of parasitised and non parasitised red blood cells.
- Malnutrition, shock, DIC leading to microangiopathic haemolysis

Hepatocyte dysfunction, which may be because of alteration in vascular flow through the organ as parasitised red blood cells adhere to endothelial cells blocking sinusoids and obstructing intrahepatic blood flow.There is evidence of focal hepatocyte necrosis, cholestasis, bile stasis, granuolomatous lesion or malarial nodules. The bile stasis is because of impairement of bilirubin transport due to endothelial blockage and disturbance of hepatocyte microvilli [18, 19.]

In acute falciparum malaria, the liver is enlarged and weighs upto 2.5 kg. It is congested and pigmented and dark brown. The predominant

histopathological changes in malarial liver comprises of a reticuloendothelial response i.e., Kupffer cell hyperplasia, presence of malarial pigement and congestion along with minor effects on hepatocytes.[20]

Additional changes in morphology include steatosis, [21] focal hepatocyte necrosis. Parasitised red blood cells are seen in Kupffer cells and endothelial cells. Characteristically rectangular, crystalline malarial pigment granules are seen in these cells. The hepatocyte contains lipofuschin and hemosiderin alongwith fat droplets deposition. The space of Disse becomes narrow with loss of microvilli of both the hepatocytes and the bile canaliculi. These last two features have been suggested as the important factors related to hepatic dysfunction and cholestasis. [18]

RENAL IMPAIRMENT

Incidence of ARF in malaria all over the world has been reported as 0.57% to 60 %. In India, the incidence of malarial ARF has been reported to be 13 % in North India, 17.8 % in New Delhi and 17.2 % in orrisa.[22]

Renal impairment is common among adults with severe falciparum malaraia but rare among children. The pathogenesis of renal failure is unclear but may be related to erythrocyte sequestration interfering with renal microcirculatory flow and metabolism. Clinically and pathologically, this syndrome manifests as acute tubular necrosis.

Acute renal failure may occur simultaneously with other vital organ dysfunction or may progress as other disease manifestations resolve.[9]

Other non specific mechanisms may come into play including hypovolemia, release of catecholamines and subsequent activation of the rennin – angiotensin system, complement activation, and rhabdomyolysis.[23] ATN is the main renal complication but latent forms of acute glomerulonephritis have also been documented.

In survivors, urine flow resumes in a median of 4 days and serum creatinine levels return to normal in a mean of 17 days.[9] Age, oliguria, central nervous system involvement and DIC emerged as bad prognostic factors in a simple univariate analysis.[24, 25]

PULMONARY INVOLVEMENT

The clinical manifestations of pulmonary involvement may start suddenly at any time during the course of malaria, even after disappearance of circulating parasites and after several days of antimalarial therapy. The mortality rate is > 80 %.[9] Pulmonary edema is the most important pulmonary manifestation of malaria.[26] It is a common feature of severe malaria.

The pathogenesis of this variant of adult respiratory distress syndrome is unclear. Capillary endothelial cells, which control the flux of fluids to the interstitial space, appear to be the most involved structure. These cells are activated by cytokines, produced by lymphocytes and

macrophages during the immune response, and express receptors and molecules of adhesion, allowing for sequestration of parasitized erythrocytes and adherence of cells, which will produce locally inflammatory mediators. The inflammatory reaction and lesion of endothelial cell that ensue together with hemodynamic alterations induced by capillary blockade due to sequestrated parasitized erythrocytes cause alterations of vascular permeability and transfer of liquid to interstitial space and alveoles. The mean central venous pressure when pulmonary edema was markedly lower in ARDS than in non – ARDS. Supporting the argument that fluid imbalance is not essential for malaria induced lung injury .[27]

ARDS in malaria can be aggravated by overly vigorous administration of intravenous fluid. [9]

ARDS are often associated with septic shock. In this situation, pneumonia and /or bacteremia should be suspected and empirically treated since they may contribute to a fatal outcome.[28]

The other presenting symptoms pertaining to pulmonary manifestations in malaria include cough, disposal, expectoration, and chest pain[29].

CEREBRAL MALARIA

Coma is a characteristic and ominous feature of falciparum malaria and is associated with mortality of 20 % despite treatment.

Lesser degrees of obtundation, delirium, and abnormal behaviour should also be taken very seriously. The onset may be gradual or sudden following a convulsion. Cerebral malaria manifests as diffuse symmetric encephalopathy; focal neurological signs are unusual.[9] Adults rarely suffer (i.e., in < 3 cases) suffer neurological sequale. Cytoadherence, malaria toxin and cytokine production have provided some evidence for both the mechanical and toxin – cytokine hypothesis to explain the pathophysiology of this condition.[30]

HYPOGLYCEMIA

Hypoglycemia is an important and common complication. It results from a failure of hepatic gluconeogenesis and an increase in the consumption of glucose by both host and to a lesser extent – the malarial parasite.

LACTIC ACIDOSIS

Lactic acidosis commonly coexists with hypoglycemia and is an important contributor to death from severe malaria. Lactic acidosis is caused by the combination of anaerobic glycolysis[31] in tissues where sequestered parasites interfere with microcirculatory flow, hypovolemia, and lactate production by the parasite and a failure of hepatic and renal lactate clearance. The prognosis of severe lactic acidosis is very poor.

FEATURES INDICATING A POOR PROGNOSIS IN SEVERE FALCIPARUM MALARIA[9]

CLINICAL

1. Marked agitation
2. Hyperventilation
3. Hypothermia (< 36.5^0 c)
4. Bleeding
5. Coma
6. Repeated convulsions
7. Anuria
8. Shock

LABORATORY

BIOCHEMISTRY

1. Hypoglycemia (< 40 mg/dl)
2. Hyperlactatemia (>5 mmol/L) Acidosis (arterial pH <7.3, serum HCO_3 <15 mmol/L)
3. Elevated serum bilirubin (>3 mg/dl)
4. Elevated serum creatinine (>3 mg/dl)
5. Elevated liver enzymes (AST/ALT 3 times upper limit of normal)
6. Elevated muscle enzymes (CPK ↑ , myoglobin ↑)
7. Elevated urate (> 600 µmol/L)

HEMATOLOGY AND COAGULOPATHY

1) Leucocytosis (>12,000 /µL)

2) Severe anemia(PCV<15%).

3) Decreased platelet count (50,000/ul)

4) Prolonged prothrombin time (>3s)

5) Prolonged partial thromboplastin time

6) Decreased Plasma Fibrinogen (100mg/dl)

PARASITOLOGY

1) Hyperparasitemia

Increased mortality at >100,000 / µL

High mortality at >500,000 /µL

20 % of parasites identified as pigment containing trophozoites and schizonts

5 % of neutrophils with visible pigment

MANAGEMENT OF SEVERE FALCIPARUM MALARIA[32, 33]

IMMEDIATE MANAGEMENT

Assess the Airway, Breathing, and Circulation and intervene when necessary.

Record the vital signs.

Assess the level of consciousness using a coma scale – the Glasgow coma scale (GCS).

Assess the state of hydration; consider catheterization of the urinary bladder and insertion of a line to measure central venous pressure.

Treat hypoglycemia.

Plan first 8 hours of intravenous fluids.

Unconscious patients should have a lumbar puncture so that CNS infections, especially acute bacterial meningitis could be excluded with certainty.

ANTI MALARIAL THERAPY FOR PL. FALCIPARUM

Anti- Malarial (Parenteral)	**Loading dose**	**Maintenance dose**
Cinchona Alkaloids		
Quinine dihydrochloride(IV)	20 mg/kg over 4 hrs	10 mg/kg over 4 hrs Repeated every 8 hrs
Artemisin derivatives		
Artesunate IV	2.4 mg/kg	1.2 mg/kg repeated at 12 & 24 hrs, then 1.2 mg/kg daily
Artemether IM	3.2 mg/kg	1.6 mg/kg repeated 12-24 hrs, then daily

SUPPORTIVE THERPAIES

FLUIDS

The role of fluids in severe falciparum malaria is controversial. Hypovolemia is corrected by bolus of fluids that improve circulation. In adults fluids must be used cautiously as they are at a greater risk of developing edema and circulatory overload. Fluid administration should be stopped and diuretics given if pulmonary edema is suspected. Monitoring the CVP is very helpful during administration of fluids. There is no evidence to show that fluid restriction improves the outcome in cerebral malaria.

BLOOD TRANSFUSION

Blood transfusion is life-saving in severe malarial anemia. The indication for blood transfusion depends on the availability of pathogen free compatible fresh blood, hemoglobin level and fluid balance status.[34] In a well–hydrated adult, a haematocrit value below 20% should be an indication for undertaking blood transfusion.

ANTICONVULSANTS

The management of seizures should include correction of the underlying cause, such as hypoglycemia. Anticonvulsants should be administered for seizures lasting for more than five minutes. Benzodiazepines are the most widely used and available anticonvulsants, but may cause respiratory depression. With repeated seizures phenytoin, phenobarbitone has been used.

HYPOGLYCEMIA

Hypoglycemia is a common complication hence frequent checking of blood glucose level is mandatory. Correction with 50 % dextrose appears to be safe in adults.

INOTROPIC SUPPORT

Although shock (Algid malaria) is rare, it is associated with death. Inotropic support may be required after correction of hypovolemia. Dopamine appears to provide better inotropic support than adrenaline in adults with severe malaria.

DIALYSIS

The indications for dialysis in acute renal failure due to severe falciparum malaria are similar to the other causes of acute renal failure. Early diagnosis of established renal failure and institution of dialysis are important in preventing mortality. A rapidly rising creatinine level is the most sensitive indicator of the need for dialysis.

VENTILATION

Prompt endotracheal intubation by experienced personnel and mechanical ventilation may be a life saving procedure. Acute respiratory distress syndrome, poor respiratory effort, aspiration pneumonia, acute pulmonary edema and deep coma may benefit from ventilator support. Care must be taken to ensure frequent suction and adequate humidification during ventilation while maintaining a $PaCO_2$ below 4.0

(KPa) since a rise in the $PaCO_2$ may increase ICP and precipitate death.

ANTIBIOTICS

In patients with a reduced level of consciousness, the differential diagnosis of meningitis must be entertained and broad spectrum anti-microbial agents should be administered until the diagnosis can be excluded. Patients put on ventilator support should also be covered with prophylactic antibiotics.

DRUG RESISTANCE IN MALARIA

In much of the tropics, drug resistant P. falciparum is increasing in distribution, frequency, and intensity. There is a growing belief among malariologists that, to prevent resistance, falciparum malaria should be treated with drug combinations and should no longer be treated with single drugs in endemic areas.

The combination strategy is based upon simultaneous use of two or more drugs with different modes of action: one usually an artemisinin derivative (artesunate, artemether, or dihydroartemisinin), given for 3 days and the other, a slower acting anti-malarial to which P.falciparum is sensitive[9.]

When the malarial parasites are fully sensitive, either amodiaquine or sulfadoxine / pyrimethamine can be used in combination with the artemisinin derivative, or amodiaquine can be combined with sulfadoxine/ pyrimethamine.

MALARIA VACCINE DEVELOPMENTS

Development of an effective and deployable malaria vaccine seems technically feasible in view of most malaria researchers. New vaccine delivery methods and adjuvants could continue to increase the antibody and cellular immunogenicity of subunit vaccination. The rate of clinical assessment of candidate malaria vaccines is increasing; in the past 5 years, the number of groups doing such research has increased from three to eleven[35].

A synthetic “cocktail” vaccine for P.falciparum, called SPf66 and developed by Dr.M. Patarroyo in Colombia[7], has been tested extensively in South America and more recently in Africa and South East Asia. A recent field among children under age 5, in the United Republic of Tanzania showed the vaccine was safe, induced antibodies and reduced the risk of developing clinical malaria by about 30%., which confirmed the potential of vaccine to confer partial protection. As far as transmission blocking vaccines are concerned Pfs25 is a leading candidate[7].

MATERIALS AND METHODS

PLACE OF STUDY

The study was carried out at Department of Medicine, Kilpauk Medical College Hospital, Kilpauk, Chennai –10.

PERIOD OF STUDY

Total period of study extended from June 2004to May 2005 (12 Months).

SAMPLE SIZE

100 consecutive Acute Falciparum malaria patients admitted in medical wards and intensive care units in Department of Medicine, Kilpauk Medical College Hospital.

TYPE OF STUDY

The study carried out was an observational and prospective clinical study.

MATERIALS AND METHODS

One hundred cases of QBC MP positive falciparum malaria (confirmed by slide positivity for asexual stage of the parasite) admitted to the medical wards and intensive care units were included in the study.

EXCLUSION CRITERIA

1. Patients below the age of 15 years.

2. Pregnant and Lactating women.

3. Patients – coexistence of both Falciparum malaria and Leptospirosis (MAST ≥ 2 +)

4. Mixed infections like associated plasmodium vivax.

A detailed history and clinical examination was carried out to note complications and assess severity after obtaining written informed consent.

The following laboratory investigations for hematological parameters were carried out: Hemoglobin estimation, Total and Differential Leucocyte count, Total Platelet count. In severe cases coagulation parameters like Bleeding time, whole blood Clotting time, Prothrombin time were done.

Biochemical investigations like blood Sugar, serum Bilirubin, Aspartate and Alanine aminotransferase, blood Urea, serum Creatinine and Electrolytes were also carried out. In patients with respiratory distress and renal failure X-ray Chest and Arterial Blood Gas Analysis were analyzed. HBsAg and Anti HCV in selected cases are done.

All patients are treated with quinine and artemisin derivatives as the prevalence of Chloroquine resistant falciparum is very high in our area.

In severe falciparum malaria cases with multisystem involvement Leptospirosis and Dengue fever were ruled out by doing MSAT & MAT and IgM & IgG antibodies for dengue respectively.

All patients were treated with antimalarials either Quinine or Artesunate depending upon clinical severity and tolerability of the patients. Other supportive measures in the form of antibiotics, anticonvulsants, antiemetics, blood transfusion inotropic support and fluids dialysis and ventilator support as and when required.

ANALYSIS OF DATA

All information pertaining to history, clinical examination, complications, relevant investigations, treatment modalities and duration of stay and also comparison of those data between mild and severe malaria were analyzed and tabulated.

Hemoglobin <11g% has been taken as Anemia, Leucocyte counts <4000 and >11000cells/µl are taken as leucopenia and leucocytosis respectively, Platelet count <1,00,000 cells/µl as thrombocytopenia. Those with Serum Creatinine >1.5mg/dl were considered as acute renal failure and they were divided into three groups Mild (S.Cr.<2mg%), Moderate (S Cr.2 to 5mg%)and Severe (S.Cr.>5mg%). Serum bilirubin > 3 mg% SGPT/SGOT > 40 IU, as liver impairment. Hypoglycemia – Blood sugar <40mg%.

WHO CRITERIA FOR SEVERE FALCIPARUM MALARIA

SYSTEMS INVOLVED	MANIFESTATIONS
Renal	Urine output (24 hrs) < 400 ml
	No improvement with rehydration
	Serum creatinine >3 mg /dl.
Respiratory	Respiratory distress.
	Pulmonary edema.
	ARDS (PaO_2/FiO_2) :< 200
	ALI (PaO_2/FiO_2) :< 300
Cardiovascular	Hypotension / Shock
	Sys. BP. < 80 mm Hg.
Neurological	Failure to localize or respond
	Appropriately to noxious stimuli;
	Coma persisting for > 30 min
	after generalized convulsion.
Hematological	Anemia
	Severe normocytic normochromic
	Hb < 5 gm/dl.
	Hct <15 %.

Liver	Jaundice Serum bilirubin > 3 mg/dl if combined with other evidence of vital organ dysfunction.
Metabolic	Hypoglycemia Plasma glucose < 40 mg/dl.
Metabolic acidosis	Arterial P^H < 7.25 Plasma bicarbonate < 15 mmo/dl.

LIMITATIONS OF THE STUDY

The main limitation of the study is that we have not done the parasitemic index and hence could not assess its relation with clinical severity and laboratorial parameters and outcome of the disease.

OBSERVATION AND ANALYSIS

PATIENT CHARACTERISTICS

1. SEX

TABLE 1

SEX	N		Mean	SD	Minimum	Maximum
Male	**Age**	59	35.7	12.9	15	63
Female	**Age**	41	40.0	15.7	15	72

A total of 100 cases smear positive for falciparum malaria were registered for the study. Out of 100 cases there were 59 males (59%), and 41 females (41%). The mean age in male was 35.7 years and female was 40.0 years.

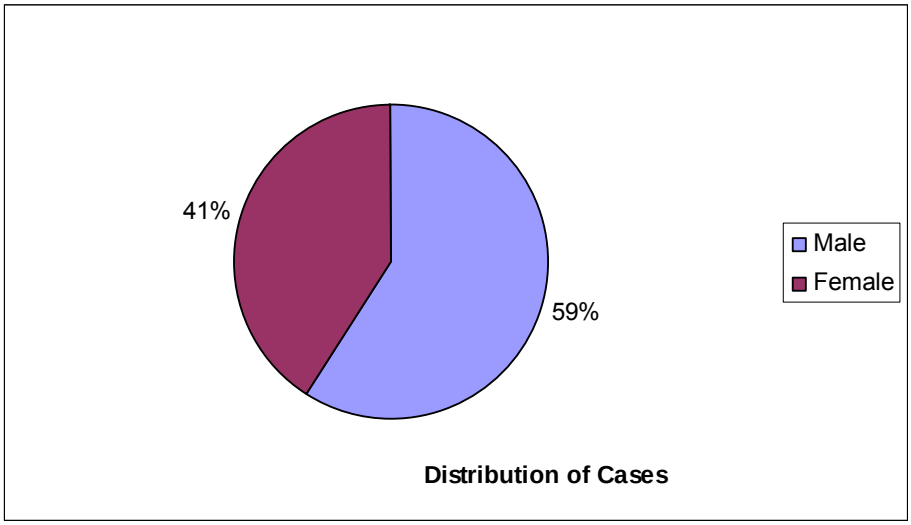

FIG.3

2. AGE.

TABLE 2

N	Valid	100
	Missing	0
Mean		37.48
Std. Deviation		14.183
Minimum		15
Maximum		72

The mean age of entire study group was 37.48, the minimum age being 15 years and the maximum age being 72 years. Maximum number of male patients was in the age group of 20 – 30 years (18%) and maximum number of female patients was in the age group of 30 – 40 years (12%) as observed from figure 4.

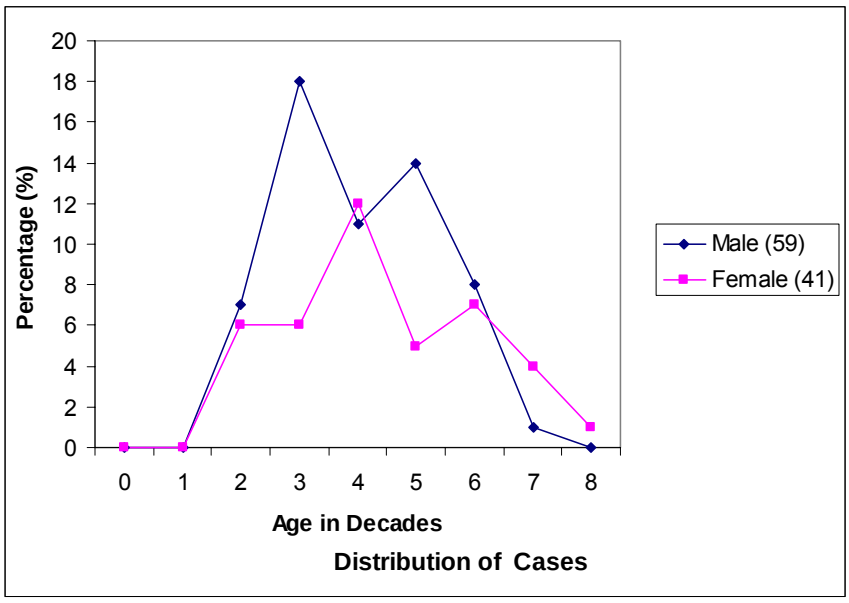

FIG.4

CLINICAL MANIFESTATIONS

The mean time from symptom onset until physician contact was 7.3 days, while the median time was 5 days. The most common clinical presentation was fever (98%), followed by nausea and vomiting. Abdominal pain was present in sixteen patients. Nine patients had diarrhea. CNS manifestations were present in nine patients. Eight patients had urinary symptoms in the form of oliguria and anuria. Three patients had bleeding manifestations.

TABLE 3

SYMPTOMS		N	% Of Patients
Fever	No	2	2.0%
	Yes	98	98.0%
Chills	No	32	32.0%
	Yes	68	68.0%
Nausea	No	70	70.0%
	Yes	30	30.0%
Vomiting	No	50	50.0%
	Yes	50	50.0%
Headache	No	72	72.0%
	Yes	28	28.0%
Myalgia	No	63	63.0%
	Yes	37	37.0%
ABDOMINAL PAIN	No	84	84.0%
	Yes	16	16.0%
DIARRHOEA	No	91	91.0%
	Yes	9	9.0%
URINARY SYM	No	92	92%
	Yes	8	8%
ALT. SENSORIUM	No	91	91%
	Yes	9	9%
BLEEDING MANIF	No	97	97.0%
	Yes	3	3.0%

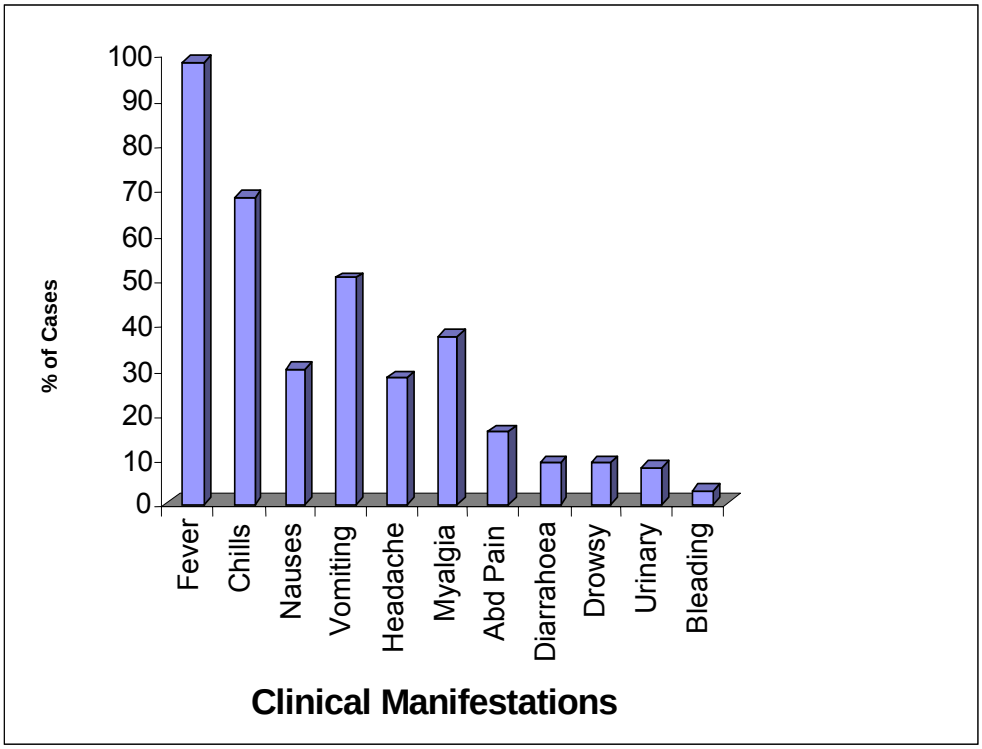
% of Cases
100
90
80
70
60
50
40
30
20
10
0
Fever
Chills
Nauses
Vomiting
Headache
Myalgia
Abd Pain
Diarrahoea
Drowsy
Urinary
Bleading
Clinical Manifestations

FIG.5

PHYSICAL SIGNS

TEMPERATURE AT THE TIME OF PRESENTATION

TABLE 4

TEMP.	NO. of PTS	
<100^{o} F	25	Mean 100.9^{o} F SD 2.04^{o} F Min 97^{o} F Max 105^{o} F
100^{o} F – 104^{o} F	69	
>104^{o} F	6	

Fever was the most common presenting complaint. It was present in 98% of cases, but only 75% had a fever on the day of presentation. The mean temperature was 100.90 F and minimum being 97 and maximum being 105 F. The fever was associated with chills in 68% of cases.

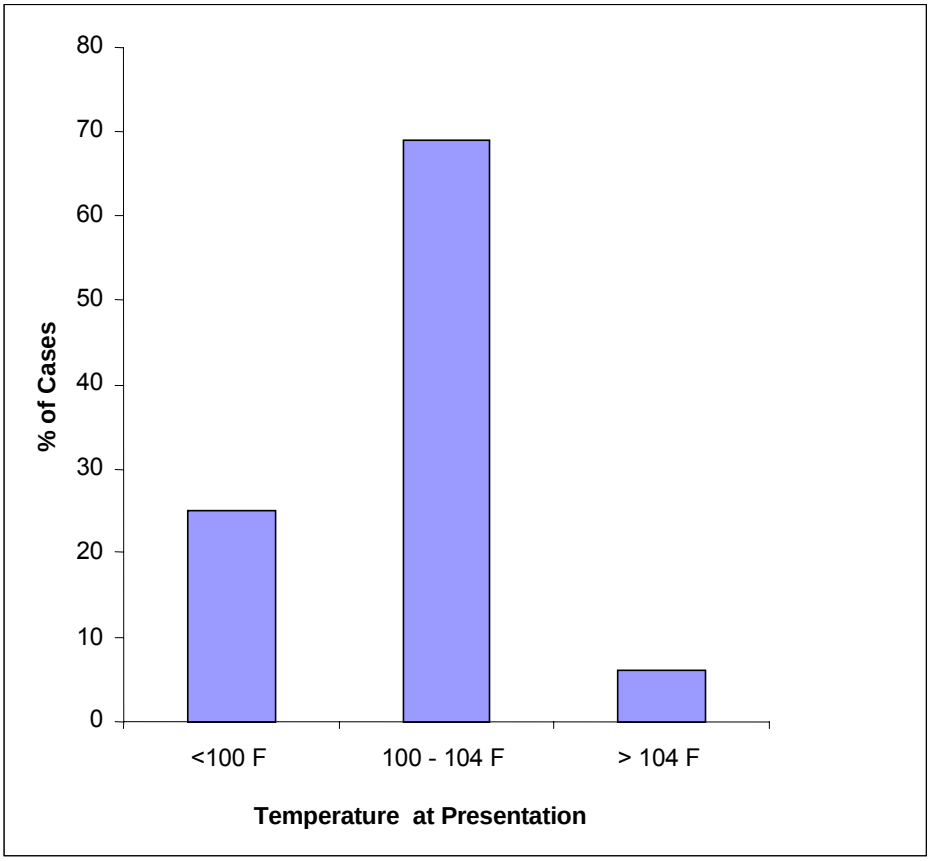
80
70
60
50
40
30
20
10
0
% of Cases
<100 F
100 - 104 F
> 104 F
Temperature at Presentation

FIG.6

SYSTOLIC BLOOD PRESSURE

TABLE 5

SYS. BP	NO. of PTS.	
<80 mm Hg	8	Mean 109.98
81– 140 mm Hg	91	SD 19.532
>141 mm Hg	1	Min 40
		Max 150

Eight patients had hypotension at the time of admission.

TABLE 6

SIGN		N	% Of Patients
Anaemic	No	75	75.0%
	Yes	25	25.0%
Icterus	No	73	73.0%
	Yes	27	27.0%
Hepatomegaly	No	80	80.0%
	Yes	20	20.0%
Splenomegaly	No	77	77.0%
	Yes	23	23.0%
Abd. tenderness	No	88	88.0%
	Yes	12	12.0%
Confusion & drowsiness	No	91	91.0%
	Yes	9	9.0%

The most common clinical signs were icterus (27%), pallor (25%), splenomegaly (23%), hepatomegaly (20%), abdominal tenderness (12%) and CNS manifestations (9%).

HEMATOLOGICAL PARAMETERS IN FALCIPARUM MALARIA:

TABLE 7

PARAMETERS	No of Cases	MEAN	SD	MIN	MAX
Hemoglobin					
Less than 5 G%	Nil				
5.1 – 7 G %	7 (7%)				
7.1 - 9 G	5 (5%)	11.3	2.3	5.5	16
9.1 – 10.9 G %	27 (21%)				
≥ 11 G %	61 (61%)				
Leucocyte count cells/µl					
Less than 4,000	30 (30 %)				
4,000 - 11,000	63 (63 %)	5,687	3,901	1,700	29,800
More than 11,000	7 (7%)				
Platelet count cells/µl					
Less than 20,000	10 (10%)				
20,000 - 50,000	29 (29%)				
51,000 - 1.00.000	39 (39%)	78,850	62,983	6,000	3,61,000
More than 1,00,000	22 (22%)				

Thrombocytopenia (78%) and anemia (39%) were the most common hematological findings. Leucopenia was noted in 30% of cases, while 7 % of cases showed leucocytosis.

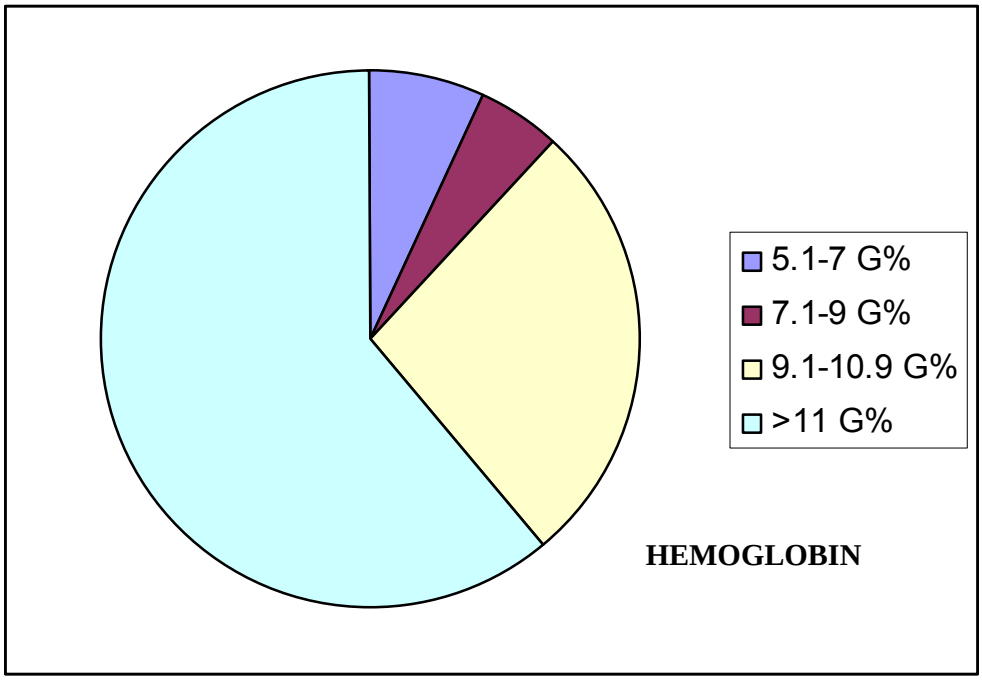

FIG. 7

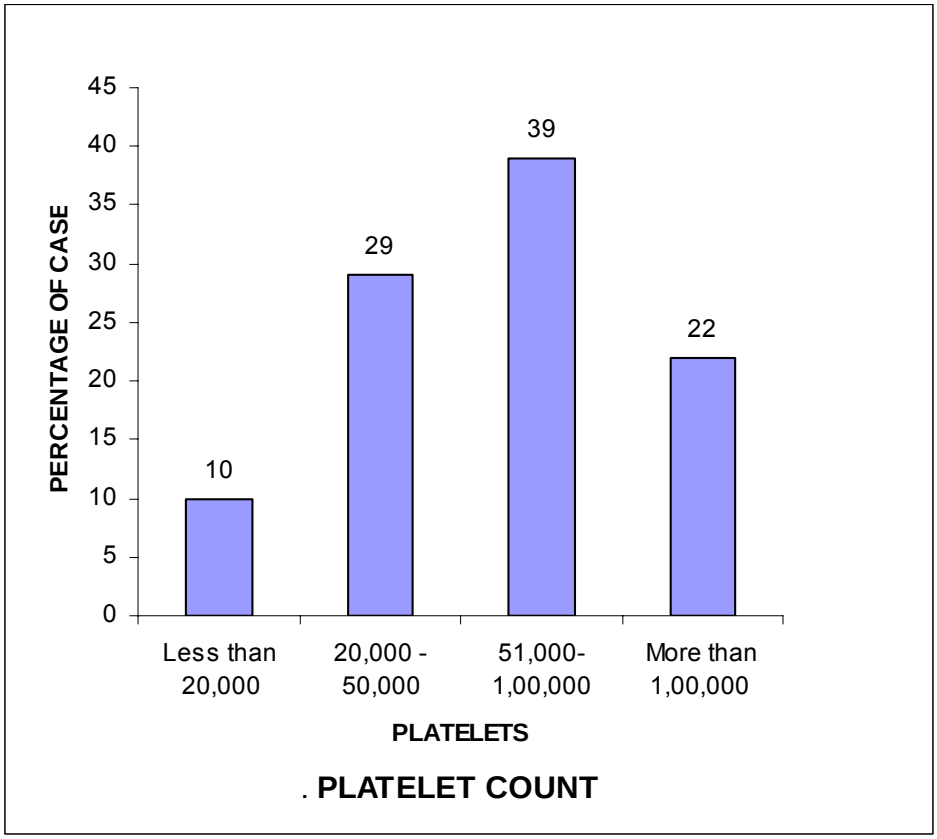
45
40
35
30
25
20
15
10
5
0
PERCENTAGE OF CASE
10
29
39
22
Less than 20,000
20,000 - 50,000
51,000- 1,00,000
More than 1,00,000
PLATELETS
. PLATELET COUNT

FIG. 8

BIOCHEMISTRY IN PATENTS CLASSIFIED AS A, B, C GROUPS ACCORDING TO SERUM BILIRUBIN LEVELS

TABLE 8

GROUPS	**A**	**B**	**C**
Serum bilirubin (mg%)	<3	3 – 10	>10
No. of patients	75	17	8
Conjugated	48	12	8
Unconjugated	27	5	-
ALT level (IU)			
<40	65	1	-
40 – 100	8	10	2
> 100	2	6	6
AST (IU)			
<40	64	2	-
40 – 100	9	12	2
> 100	2	3	6
Mortality			
No. of patients	75	17	8
Deaths	-	-	4
Percentage	-	-	50%

25 % of patients had serum bilirubin more than 3 mg%.

BIOCHEMICAL CHANGES - RENAL FUNCTION

TABLE 9

BLOOD UREA		
Up to 40 mg %	63 (63%)	MEAN – 46.8 SD – 59.1 MIN- 10 MAX -507
41 – 80 mg %	27 (27%)	
More than 80 mg %	10 (10%)	

TABLE 10

SERUM CREATININE		
NORMAL (< 1.5 mg%)	89 (89%)	Mean --1.18 SD – 1.5 MIN. – 0.5 MAX. – 15.2
1.5 – 3 mg %	9 (9%)	
MORE THAN 3 mg %	2 (2 %)	

TIME TAKEN - RISE IN PLATELET COUNT (81 CASES)

TABLE 11

Days after Admn.	% of Cases	
1 to 5 Days	48	Mean 5.8
6 to 10 Days	31	SD 2.2
> 10 Days	2	Min 1
		Max 15

TABLE 12

TOTAL DURATION OF STAY

NO OF DAYS	NO OF PATIENTS	
1 to 5 Days	45	Mean 6.32
6 to10 Days	50	SD 2.28
> 10 Days	5	Min 1
		Max 15

DISCUSSION

This study was a prospective clinical observational study done for a period of 12 months from June 2004to May 2005 Its objectives were to study the common clinical presentations and also atypical presentation if any of acute plasmodium falciparum malaria, to assess life threatening complications of severe malaria and to collect a detailed hematological and biochemical profile of acute falciparum malaria with objective of noting its abnormalities and correlation if any with clinical severity and prognosis.

A total 100 cases of fever positive for malarial parasite by QBC method and confirmed for falciparum malaria by slide positive for asexual stage of Plasmodium faciparum who were admitted in medical wards and ICU ward at Department of Medicine, Kilpauk Medical College Hospital are taken. Our reference study which was conducted by Murthy GL. Sahay RK. Srinivasan VR. Upadhaya AC. Shantaram V. Gayatri K. (158 patients) was published in Journal of the Indian Medical Association Apr 2000.[36.]

The mean age of presentation was 37.48 years (SD 14.18). In males the mean age was 35.7 years (SD12.9) and in females the mean age of presentation was 40.0 years (SD 15.7) which was similar to Murthy et al where it was 38.60 years (SD 15.45). Majority of cases were males 59% and 41% were females. In Murthy et al., it was also predominantly of male population (69.62%).

The commonest presenting manifestations were fever (98%), fever with chills and rigors (68%), followed by vomiting (50%), myalgia (37%), , headache (28%), and icterus (27%) The other less common manifestations are abdominal pain (16%), diarrhea (9%), altered sensorium (9%), urinary symptoms (8%). hypotension (8%) and bleeding manifestations (3%).

The most frequently encountered complication is thrombocytopenia (78%) as against Murthy et al, in which it was (40.50%). In other studies like UM Jadhav, et al., and Sharma SK et al, the incidence of thrombocytopenia were 78.4% and 90% of cases respectively which are very similar to our study and also highlights the fact that a persistent normal platelet count is unlikely in the laboratory findings of malaria.

The thrombocytopenia was rarely accompanied by clinical bleeding or biochemical evidence of DIVC. Ten percent of patients had platelet counts below 25,000/µl. Platelet counts rise rapidly with recovery. Mean duration for recovery of platelet count was 5.8 days (SD 2.2). Two patients took more than 10 days for recovery and the maximum duration was 15 days. Thrombocytopenia was seen in 40-90 % of patients infected with P. falciparum infection in India.

The incidence of anemia in our study is 39%, as against 74.68% in Murthy et al., and 86.7% cases in Sharma SK et al. The incidence of leucopenia was 30% which was higher than Sharma SK et al, which

had 6.7% and leucocytosis in our study was 7 % which was slightly lower than that of Sharma SK et al (13%).

The incidence of acute renal failure in our study is 10% (Mild =3%, Moderate =6%, Severe=1%), as against 24.68% in Murthy et al. and similar to 4% of patients in Mehta KS et al. 40% of patients required dialysis in our study as against 92% in Mehta KS et al. Six patients had oliguria and 2 patients had anuria. Among patients with altered renal parameters mean urea on admission was 92.25 mg% (SD 88.58), maximum being 507 mg%. Maximum creatinine on admission was 15.2 mg%. Two patients underwent hemodialysis.

The incidence of malarial hepatopathy in our study is 25% where as it was 40.5% in Murthy et al. and 64% in DK. Kochar et al[18]. 17 % had bilirubin between 3 to 10mg/dl and 8 % had bilirubin more than 10mg/dl and the maximum bilirubin was 29.5mg/dl which are similar to DK.Kochar et al. According to WHO the patients of severe falciparum malaria with jaundice rarely have serum bilirubin levels of more than 10mg%. Of the 8 cases of severe hyperbilirubinemia 4 cases died which may indicate a good prognostic marker.

In our study we also observed raised serum liver enzyme levels in some of the patients. 75 % patients having bilirubin levels more than 10mg% also had very high levels of serum enzymes which are similar to DK. Kochar et al. which had raised enzyme levels in 75 % patients with more than 10mg%. Earlier Chawla et al and Anand et al also had similar observations in patients of falciparum malaria.

In our study 2% patients developed ARDS and ALI in 1% patient which is similar to 4% patients in Rajput R et al[29]. All developing ARDS expired as in Rajput et al. Acute lung injury is more likely to occur in patients with extremely severe, multisystemic P. falciparum malaria. Prior antibiotic treatment does not change the incidence of ARDS due to falciparum malaria.

In our study 9% of patients had cerebral malaria as against 45.56% in Murthy et al. but was similar to 12.5% in Gopinathan VP .et al.[37] Metabolic acidosis was present in 6% of patients. The degree of the metabolic acidosis in falciparum malaria correlates positively with disease severity.

Out of the 6 patients presented with metabolic acidosis 5 patients had renal failure. The minimum P^H was 6.538 but it was seen in non renal failure case. The minimum P^H in renal failure patients was 6.926.

Out of 100 cases 8 % presented with hypotension, all the patients presented with multi system involvement. 4 patients died among them and 4 patients were managed with IV fluids and inotropic support.

Among the 3 patients presented with bleeding manifestations one patient had normal bleeding time, coagulation time and prothrombin time with platelet count being 44,000 cells/dl. Another patient had multisystem involvement with increased prothrombin time and platelet count being 36,000 cells/dl.

In our study 1 patient presented with acute abdomen without fever and mimicked acute appendicitis. Another had pancytopenia without fever with a bleeding manifestation (epistaxis).

The overall mortality in our study was 4% all of which were due to MODS (MULTI ORGAN DYSFUCTION SYNDROME). This coincides with D.K.Kochar study, the leading cause of death in 2001 was MODS with predominant presentation of jaundice and renal failure.[38]

COMPARISON OF PROFILE WITH OTHER STUDIES

Variables	Our study (%)	Murthy et al (%)	Other studies (%)
Fever	98	98.1	100(Nityan et al)[39]
Fever,chills and rigors	68	98.1	
Icterus	27	27.21	46.6(Nityan et al)
Diarrhoea	9		10(Nityan et al)
Algid malaria	8	18.35	
Renal failure	10	24.68	33.3(Habte et al)[40]
Cerebral malaria	9	45.56	12.5(Gopinathanetal) 46.6(Nityan et al)
Anemia	39	74.68	86.7(Sharma et al) 78.3(Nityan et al)
Thrombocytopenia	78	40.50	78.4(Jadhav et al) 90(Sharma et al)
Leucocytosis	7	-	13.3(Sharma et al)
Leucopenia	30	-	6.7(Sharma et al)
Bilirubin >10mg%	8	-	24 (Kochar et al)
SGOT/SGPT>100IU/L	36	-	24 (Kochar et al)
ARDS/ALI	3	-	15.1(Rajput et al)
Bleeding Compl.	3	4.43	
Mortality	4	20.25	12(Kochar et al)

SUMMARY

1) An observational and prospective study was carried out from June 2004to May 2005 at Department of Medicine, Kilpauk Medical College Hospital, Kilpauk, Chennai –10, with objectives of finding the common clinical presentation of Falciparum malaria and if any atypical presentation, hematological and biochemical parameters and their association with disease severity and complications and prognostic indicators.

2) 100 cases of fever, positive for malarial parasite by QBC method and confirmed for falciparum malaria by slide positive for asexual stage of P.falciparum were recruited into the study and followed.

3) In our study males predominated accounting for 59% of cases and females were 41%.

4) The mean age group in our study population was 37.48 years (SD 14.18), maximum age being 72 years. Among male group the mean age was 35.7years (SD 12.9), maximum age being 63 years. Most male patients' age group was between 2^{nd} and 3^{rd} decade. In female group the mean age was 40.0 years (SD 15.7), the maximum being 72 years. Most female patients age group between 4^{th} and 5^{th} decade.

5) The mean time from symptom onset until physician contact was 7.3 days while the median time was 5 days.

6) The most common clinical presentation was fever and it was present in 98% of cases. However it was associated with chills and rigor only in 68% of cases. 25% of patients were afebrile at the time of presentation. The fever does not follow a classic tertian pattern. The mean temperature was 100.9 F (SD 2.04) and the maximum being 105 F.

7) The next common presentation was vomiting (50%) followed by myalgia (37%), headache (28%), abdominal pain (16%) and diarrhea (9%). 9% had CNS manifestations and 8% had urinary symptoms.

8) Among 2 patients (2%), without fever one had abdominal pain and vomiting mimicking acute appendicitis. Another patient had bleeding from nose.

9) The commonest clinical sign apart from fever was icterus (27%) followed by pallor (25%). splenomegaly (23%) and hepatomegaly (20%)

10) The most common hematological abnormality was thrombocytopenia (78%), with mean of 78,850/µl (SD 62,983), the minimum being 6000/µl and the maximum being 3,61,000/µl. 39% of cases had platelet count < 50,000/µl. Three patients had undergone platelet transfusion.

11) Anemia was present in 39 % of cases and mean Hb 11.3 g% (SD 2.3), the minimum being 5.5 g%. Five patients had undergone

blood transfusion for Hb less than 7 gm%. Leucopenia (30%) and Leucocytosis (7%) were noted in our study.

12) Liver impairment was noted in 25% of cases with bilirubin more than 3 mg%. 8% of patients had bilirubin more than 10mg%. The maximum bilirubin was 29.5mg%. Conjugated hyperbilirubinemia was noted in 20% of cases. ALT and AST were raised in 24% and 23% cases respectively. Mortality was noted in cases with bilirubin more than 10 mg%.

13) As per WHO criteria of sever falciparum malaria renal failure was noted only in 2% of cases with serum creatinine more than 3 mg%. One patient had creatinine 15.2 mg% and we could not dialyse as the patient had hypotension. Another patient had creatinine 3.3 mg% and was managed conservatively.

14) Among patients with creatinine less than 3 mg%, we had 6% of patients with urea more than 100 mg% and 2 % patients had urea more than 80 mg%. In patients with urea more than 100 mg %, two patients had urea 180mg % and 176mg % with their creatinine being 2.5 mg % and 2.7 mg% respectively. Both had hypotension and were oliguric. After BP was stabilized with IV fluids and inotropic support they were taken up for dialysis, but could not be saved.

15) Eight (8%) had hypotension at the time of presentation.

16) Six (6%) patients had metabolic acidosis. Among them 5 had liver impairment, 4 had hypotension, and 4 had renal involvement. Two of them undergone hemodialysis.

17) Nine (9%) patients had features of cerebral involvement .

18) 2 % of patients developed ARDS and one patient developed ALI. Mortality was 100 % in ARDS group.

19) 2 % patients had hypoglycemia which was managed with 50% dextrose.

20) Mortality rate was 4 % in our study group. All of them had hypotension metabolic acidosis, liver impairment and cerebral involvement. Renal impairment was noted among 3%. 2% of them had ARDS.

CONCLUSIONS

1. The commonest clinical presentation is fever which is continuous and irregular but it has not followed a tertian pattern.

2. The commonest hematological abnormality is thrombocytopenia followed by anemia.

3. Thrombocytopenia is rarely accompanied by clinical bleeding and has therapeutic implications in context of avoiding unnecessary Platelet infusions.

4. Very severe anemia is not a common presenting feature in falciparum malaria in the study group.

5. In our study the evidence of predominantly conjugated hyperbilirubinemia and increased levels of SGOT, SGPT levels suggest gross hepatocytic dysfunction in patients of Plasmodium falciparum malaria with jaundice.

6. Patients developing ARDS has 100 % mortality.

7. Factors associated with high mortality are renal failure, hypotension, metabolic acidosis, severe liver dysfunction, cerebral involvement and ARDS.

8. In Chennai, Falciparum malaria should be included in the differential diagnosis whenever a patient is admitted for fever with MULTI ORGAN DYSFUNCTION.

PROFORMA

Name: Age: Sex:

Registration no:

Address:

Date of admission:

Date of discharge:

Presenting complaints:

Fever – duration

Chills and rigor

Nausea and vomiting

Myalgia and headache

Diarrhea

Abdominal pain

Jaundice

Oliguria / Anuria

Altered sensorium

Bleeding manifestations

PHYSICAL EXAMINATION :

Temp. At admn. :

Pulse rate:

Blood pressure:

Respiratory rate:

Anemia:

Icterus:

CVS:

RS:

Hepatomegaly:

Splenomegaly:

Abdominal tenderness:

CNS exam. :

INVESTIGATIONS:

Hematological:

Hb %: PCV. :

Leucocyte count: Total: Differential:

Platelet count: At admn. : At dis. :

LIVER FUNCTION TESTS:

Bilirubin: Total: Direct: Indirect:

SGOT: SGPT:

Total protein: Albumin: Globulin:

RENAL FUNCTION TESTS:

Blood Urea:

Serum Creatinine:

Urine Albumin: Sugar: Deposits:

Blood sugar:

SELECTIVE / SEVERE CASES:

Coagulation:

Bleeding time:

Coagulation time:

Prothrombin time:

INR:

Arterial Blood Gas analysis:

X – Ray chest:

ECG:

Leptospirosis : MAST : MAT :

Dengue : IgM: IgG :

HBsAg: Anti HCV:

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